

WEST Search History

DATE: Friday, January 19, 2007

| Hide? | Set Name | Query | Hit Count |
|--------------------------|----------|---|-----------|
| | | <i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ</i> | |
| <input type="checkbox"/> | L1 | VITAMIN d | 14410 |
| <input type="checkbox"/> | L2 | 2-METHYLENE-19-NOR VITAMIN d | 1 |
| <input type="checkbox"/> | L3 | 2-METHYLENE-19-NOR VITAMIN d | 1 |
| <input type="checkbox"/> | L4 | 2-ALKYLIDENE 19-NOR VITAMIN d | 2 |
| <input type="checkbox"/> | L5 | L4 AND LIFE EXPECTANCY | 0 |

END OF SEARCH HISTORY

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research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:30:52 ON 19 JAN 2007

=> EGISTRY

EGISTRY IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 13:31:08 ON 19 JAN 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 18 JAN 2007 HIGHEST RN 917867-30-2

DICTIONARY FILE UPDATES: 18 JAN 2007 HIGHEST RN 917867-30-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> S 235108-14-2/RN

L1 1 235108-14-2/RN

=> S 213319-29-0/RN

L2 1 213319-29-0/RN

=> S 2133250-70-5/RN

L3 0 2133250-70-5/RN

=> S 213250-70-5/RN

L4 1 213250-70-5/RN

=> D L1 AND L2 AND L4

L2 IS NOT VALID HERE

For an explanation, enter "HELP DISPLAY".

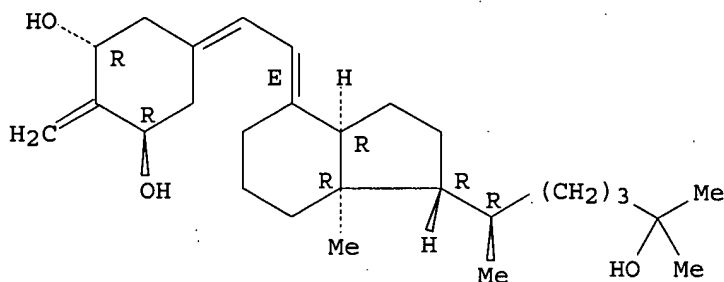
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=> D L1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 235108-14-2 REGISTRY
ED Entered STN: 26 Aug 1999
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,14 β)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

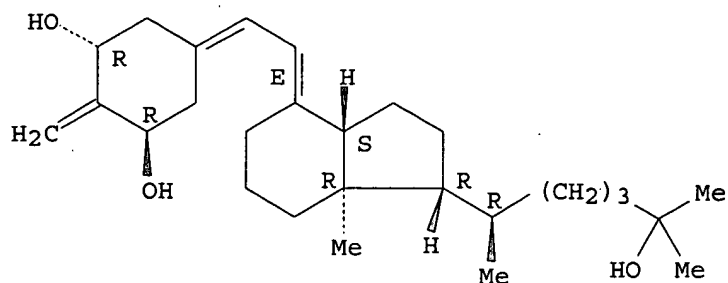
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> D L2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 213319-29-0 REGISTRY
ED Entered STN: 28 Oct 1998
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E)-(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1R)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

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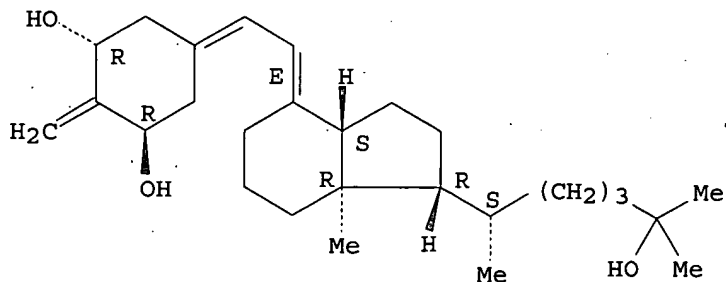
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

29 REFERENCES IN FILE CA (1907 TO DATE)
29 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> D L4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 213250-70-5 REGISTRY
ED Entered STN: 27 Oct 1998
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1α,3β,7E,20S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1,3-Cyclohexanediol, 2-methylene-5-[(2E)-[(1R,3aS,7aR)-octahydro-1-[(1S)-5-hydroxy-1,5-dimethylhexyl]-7a-methyl-4H-inden-4-ylidene]ethylidene]-, (1R,3R)-
CN 2-Methylene-19-nor-20(S)-1α,25-dihydroxyvitamin D3
CN 2MD
FS STEREOSEARCH
MF C27 H44 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, IMSDRUGNEWS, IMSRESEARCH, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

48 REFERENCES IN FILE CA (1907 TO DATE)
48 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> FILE CAPLUS
COST IN U.S. DOLLARS

| SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|
| 8.10 | 8.31 |

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:33:54 ON 19 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 19 Jan 2007 VOL 146 ISS 5
FILE LAST UPDATED: 18 Jan 2007 (20070118/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> S L1 AND L2 AND L4

1 L1

29 L2

48 L4

L5 0 L1 AND L2 AND L4

=> 1 L1

1 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> S L1

L6 1 L1

=> S L2

L7 29 L2

=> S L4

L8 48 L4

=> S L7 AND L8

L9 27 L7 AND L8

=> S L1 OR L2 OR L4 AND CANCER

1 L1

29 L2

48 L4

303251 CANCER

L10 34 L1 OR L2 OR L4 AND CANCER

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=> D L10 1-34 IBIB HITSTR ABS

L10 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:283341 CAPLUS

DOCUMENT NUMBER: 142:310363

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of hypocalcemic tetany or hypoparathyroidism

INVENTOR(S): Miller, Jeffrey Wells; Nduaka, Chudi Ike

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

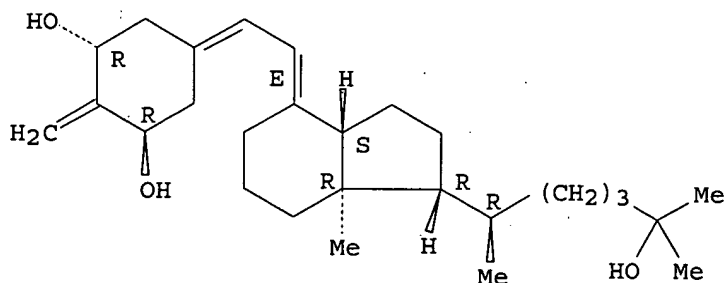
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|----------|-----------------|------------|
| WO 2005027928 | A1 | 20050331 | WO 2004-IB2910 | 20040906 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005101578 | A1 | 20050512 | US 2004-943562 | 20040916 |
| PRIORITY APPLN. INFO.: | | | US 2003-504022P | P 20030919 |
| IT 213319-29-0P | | | | |
| RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) | | | | |
| (preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of hypocalcemic tetany or hypoparathyroidism) | | | | |
| RN 213319-29-0 | CAPLUS | | | |
| CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating hypocalcemic tetany

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or hypoparathyroidism, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating hypocalcemic tetany or hypoparathyroidism, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:283340 CAPLUS

DOCUMENT NUMBER: 142:341912

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and an estrogen agonist/antagonist

INVENTOR(S): Lee, Andrew George

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|------------------|------------|
| WO 2005027924 | A1 | 20050331 | WO 2004-IB2900 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2004273658 | A1 | 20050331 | AU 2004-273658 | 20040906 |
| CA 2539361 | A1 | 20050331 | CA 2004-2539361 | 20040906 |
| EP 1667692 | A1 | 20060614 | EP 2004-769299 | 20040906 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | |
| CN 1852720 | A | 20061025 | CN 2004-80026832 | 20040906 |
| BR 2004014448 | A | 20061114 | BR 2004-14448 | 20040906 |
| US 2005070512 | A1 | 20050331 | US 2004-943568 | 20040916 |
| NO 2006001702 | A | 20060619 | NO 2006-1702 | 20060418 |
| PRIORITY APPLN. INFO.: | | | US 2003-504521P | P 20030919 |
| | | | WO 2004-IB2900 | W 20040906 |

IT 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical combinations of 2-alkylidene-19-nor-vitamin D derivs. and an estrogen agonist/antagonist)

RN 213319-29-0 CAPLUS

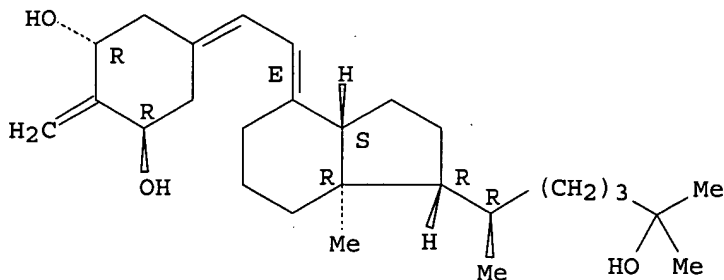
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an estrogen agonist/antagonist or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-Ia, 25-dihydroxyvitamin D3 and (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydronaphthalene-2-ol, or a pharmaceutically acceptable salt or prodrug thereof.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:283339 CAPLUS

DOCUMENT NUMBER: 142:310362

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of rickets or vitamin D deficiency

INVENTOR(S): Miller, Jeffrey Wells; Nduaka, Chudi Ike

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005027920 | A1 | 20050331 | WO 2004-IB2925 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

US 2005101577 A1 20050512 US 2004-942382 20040916

PRIORITY APPLN. INFO.: US 2003-503811P P 20030919

IT 213319-29-OP

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

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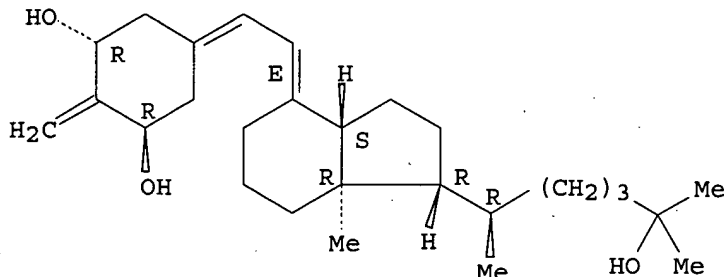
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for the treatment of rickets or vitamin D deficiency)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating vitamin D deficiency, particularly rickets, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating vitamin D deficiency with 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259681 CAPLUS

DOCUMENT NUMBER: 142:317006

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a growth hormone secretagogue

INVENTOR(S): Lee, Andrew G.

PATENT ASSIGNEE(S): Pfizer Inc, USA

SOURCE: U.S. Pat. Appl. Publ., 23 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065180 | A1 | 20050324 | US 2004-942376 | 20040916 |
| WO 2005027913 | A1 | 20050331 | WO 2004-IB2899 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, | | | |

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SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-504001P

P 20030919

IT 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

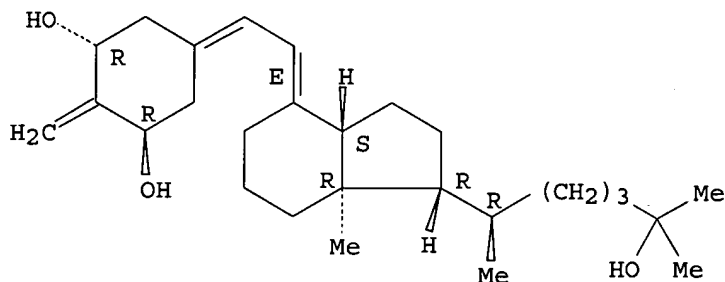
(preparation 2-methylene-19-norvitamin D derivs. for use in compns. with a growth hormone secretagogue)

RN 213319-29-0 CAPLUS

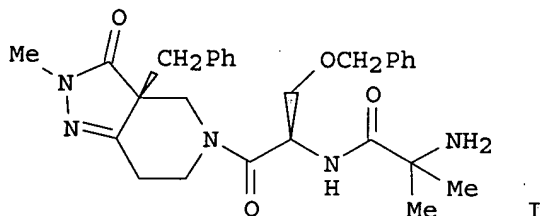
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



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AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and a growth hormone secretagogue or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃ and a growth hormone secretagogue (e.g. I) or a pharmaceutically acceptable salt or prodrug thereof.

L10 ANSWER 5. OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259665 CAPLUS

DOCUMENT NUMBER: 142:310360

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of anorexia or low bone mass in females exhibiting aggressive athletic behavior

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

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SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065134 | A1 | 20050324 | US 2004-944368 | 20040916 |
| WO 2005027925 | A1 | 20050331 | WO 2004-IB2904 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-504510P P 20030919

OTHER SOURCE(S): CASREACT 142:310360

IT 213319-29-0P

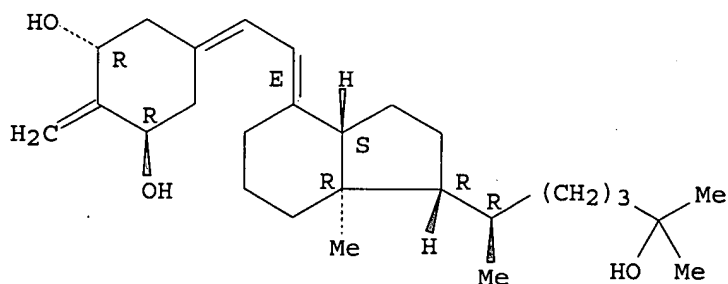
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of anorexia or low bone mass in females exhibiting aggressive athletic behavior)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating anorexia or low bone mass in females exhibiting aggressive athletic behavior, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxy-vitamin D3.

L10 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

10669990

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ACCESSION NUMBER: 2005:259664 CAPLUS
DOCUMENT NUMBER: 142:317005
TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin d derivatives and an ep2 or ep4 selective agonist
INVENTOR(S): Lee, Andrew G.; Thompson, David D.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065133 | A1 | 20050324 | US 2004-944119 | 20040916 |
| WO 2005027931 | A1 | 20050331 | WO 2004-IB2949 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-503798P P 20030919

IT 213250-70-5P 213319-29-0P

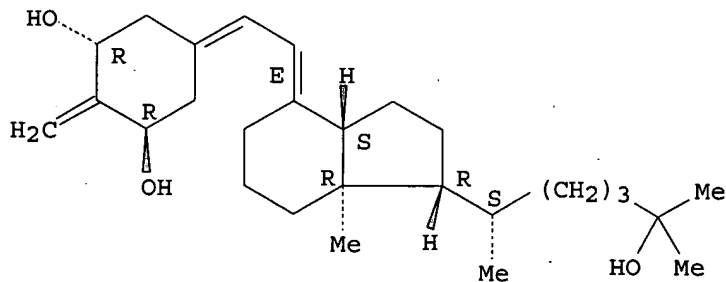
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS

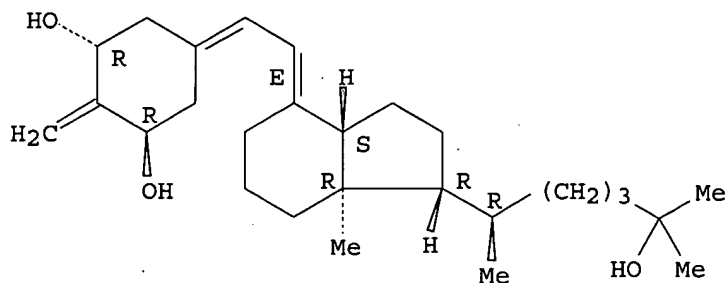
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10669990

QAZI

Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an EP2 or EP4 selective agonist or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃ and an EP2 or EP4 selective agonist or a pharmaceutically acceptable salt or prodrug thereof.

L10 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259663 CAPLUS

DOCUMENT NUMBER: 142:310359

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment or prevention of a second hip fracture

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065132 | A1 | 20050324 | US 2004-944065 | 20040916 |
| WO 2005027919 | A1 | 20050331 | WO 2004-IB2914 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-504004P P 20030919

OTHER SOURCE(S): CASREACT 142:310359

IT 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

QAZI

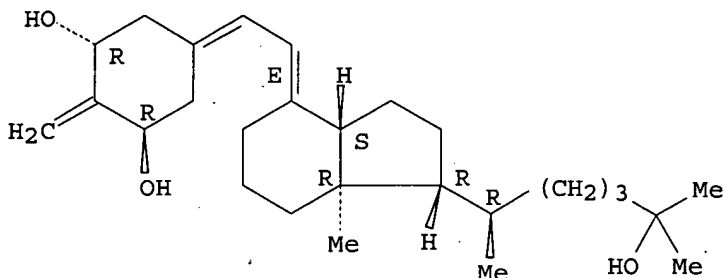
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment or prevention of a second hip fracture)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



AB The present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating or preventing a second hip fracture, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D 3.

L10 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259662 CAPLUS

DOCUMENT NUMBER: 142:310358

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for enhancement of peak bone mass in adolescence

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065131 | A1 | 20050324 | US 2004-944063 | 20040916 |
| WO 2005027927 | A1 | 20050331 | WO 2004-IB2906 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.:

US 2003-504511P

P 20030919

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OTHER SOURCE(S): CASREACT 142:310358

IT 213319-29-0P

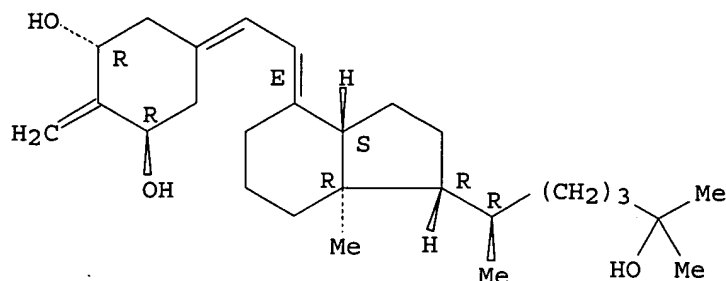
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for enhancement of peak bone mass in adolescence)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of enhancing peak bone mass in adolescence, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D3.

L10 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259661 CAPLUS

DOCUMENT NUMBER: 142:336520

TITLE: Preparation, pharmaceutical compositions, and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a cyclooxygenase-2 inhibitor

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065130 | A1 | 20050324 | US 2004-943561 | 20040916 |
| WO 2005027918 | A1 | 20050331 | WO 2004-IB2913 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, | | | |

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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-504003P

P 20030919

IT 213250-70-5P 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

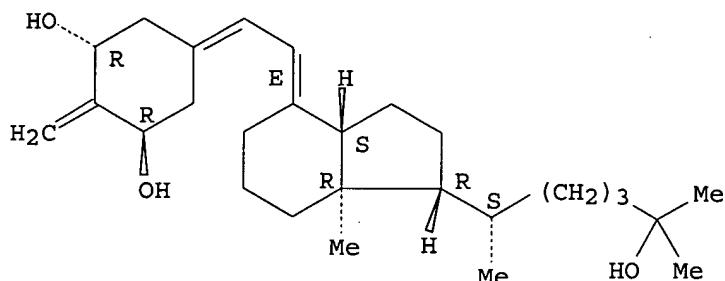
(preparation of and pharmaceutical compns. and methods comprising
combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase
inhibitors)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

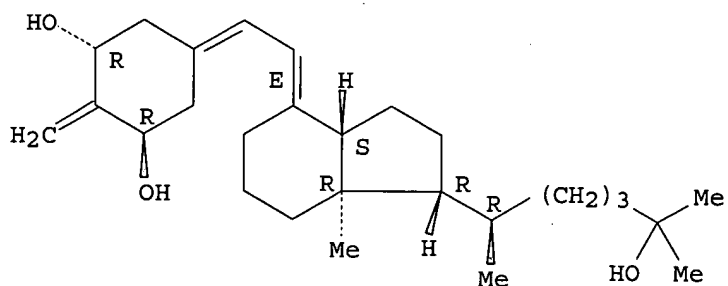


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

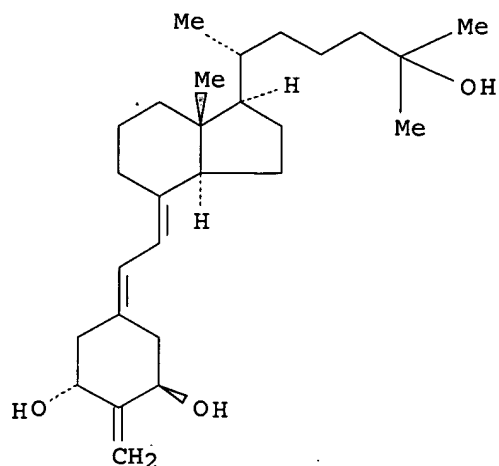
Double bond geometry as shown.



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AB The invention relates to pharmaceutical compns., and methods of treatment comprising administering to a patient in need of a combination of a 2-alkylidene-19-nor-vitamin D derivative and a cyclooxygenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need of 2-methylene-19-nor-20(S)-10,25-dihydroxyvitamin D3 and a cyclooxygenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Thus, 1α,25-dihydroxy-2-methylene-19-norvitamin D3 (I) was prepared in 11 steps from (-)-quinic acid. and (20S)-1α,25-dihydroxy-2-methylene-19-norvitamin D3 was prepared from (20S)-25-[(triethylsilyl)oxy]-des-A,B-cholestan-8-one in 4 steps.

L10 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259660 CAPLUS

DOCUMENT NUMBER: 142:310357

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of frailty, muscle damage or sarcopenia

INVENTOR(S): Lee, Andrew G.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005065129 | A1 | 20050324 | US 2004-943553 | 20040916 |
| AU 2004273659 | A1 | 20050331 | AU 2004-273659 | 20040906 |
| CA 2538993 | A1 | 20050331 | CA 2004-2538993 | 20040906 |
| WO 2005027914 | A1 | 20050331 | WO 2004-IB2901 | 20040906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

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TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1667688 A1 20060614 EP 2004-769300 20040906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

CN 1852718 A 20061025 CN 2004-80027153 20040906

BR 2004014564 A 20061107 BR 2004-14564 20040906

NO 2006001704 A 20060619 NO 2006-1704 20060418

PRIORITY APPLN. INFO.: US 2003-504509P P 20030919
WO 2004-IB2901 W 20040906

IT 213319-29-0P

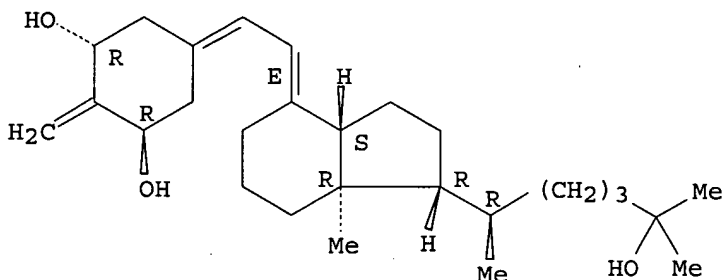
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for the treatment of
frailty, muscle damage or sarcopenia)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating frailty, muscle
damage or sarcopenia, the methods comprising administering to a patient in
need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the
present invention relates to methods of treating frailty, muscle damage or
sarcopenia, the methods comprising administering to a patient in need
thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-
1 α ,25-dihydroxyvitamin D₃.

L10 ANSWER 11 OF 34 CAPLUS. COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259659 CAPLUS

DOCUMENT NUMBER: 142:310356

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D
derivatives for the treatment of hypogonadism or
andropause

INVENTOR(S): Campagnari, Judith L.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

10669990

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PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065128 | A1 | 20050324 | US 2004-943059 | 20040916 |
| WO 2005027922 | A1 | 20050331 | WO 2004-IB2937 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-503810P P 20030919

OTHER SOURCE(S): MARPAT 142:310356

IT 213319-29-0P

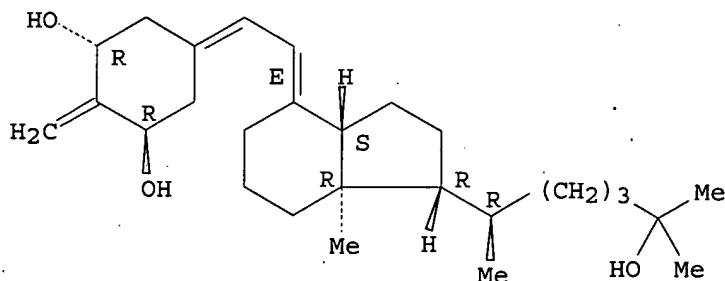
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of hypogonadism or andropause)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating hypogonadism or andropause, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating hypogonadism or andropause, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D 3.

L10 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259658 CAPLUS

DOCUMENT NUMBER: 142:310355

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of osteosarcoma

INVENTOR(S): Campagnari, Judith L.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

10669990

QAZI

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005065127 | A1 | 20050324 | US 2004-942704 | 20040916 |
| WO 2005027930 | A1 | 20050331 | WO 2004-IB2918 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-504021P P 20030919

OTHER SOURCE(S): MARPAT 142:310355

IT 213319-29-0P

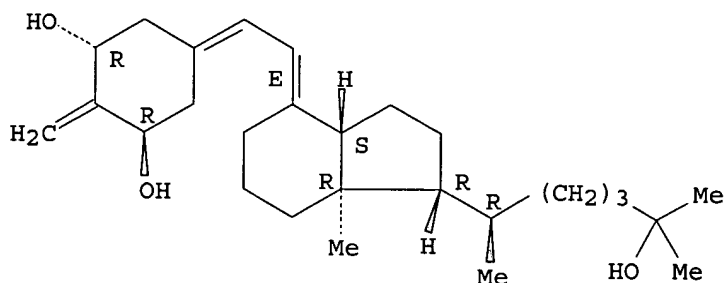
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of osteosarcoma)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to methods of treating osteosarcoma, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating osteosarcoma, the methods comprising administering to a patient in need thereof a therapeutically effective amount of 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D 3.

L10 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259657 CAPLUS

DOCUMENT NUMBER: 142:317004

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and aromatase inhibitors

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INVENTOR(S): Lee, Andrew G.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 19 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005065126 | A1 | 20050324 | US 2004-942613 | 20040916 |
| WO 2005027916 | A1 | 20050331 | WO 2004-IB2903 | 20040906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-504005P P 20030919

IT 213250-70-5P 213319-29-0P

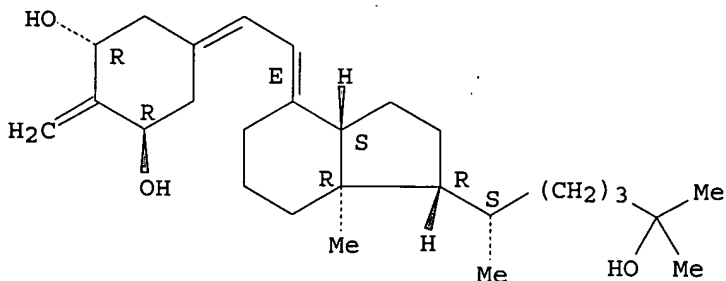
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

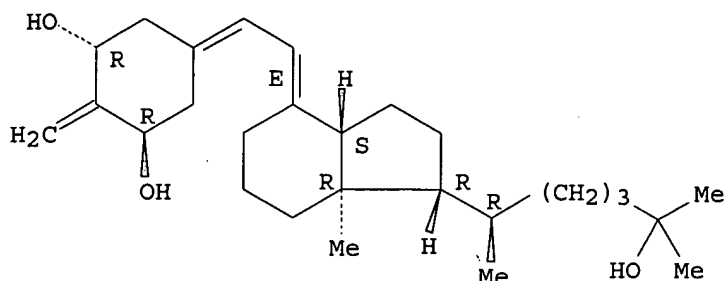


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

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AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an aromatase inhibitor. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D3 and an aromatase inhibitor.

L10 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259656 CAPLUS

DOCUMENT NUMBER: 142:310354

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D derivatives for the treatment of osteopenia or male osteoporosis

INVENTOR(S): Campagnari, Judith L.; Lee, Andrew G.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| US 2005065125 | A1 | 20050324 | US 2004-942377 | 20040916 |
| AU 2004273667 | A1 | 20050331 | AU 2004-273667 | 20040906 |
| CA 2539358 | A1 | 20050331 | CA 2004-2539358 | 20040906 |
| WO 2005027917 | A1 | 20050331 | WO 2004-IB2912 | 20040906 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1667690 | A1 | 20060614 | EP 2004-769311 | 20040906 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| CN 1852717 | A | 20061025 | CN 2004-80026946 | 20040906 |
| BR 2004014465 | A | 20061114 | BR 2004-14465 | 20040906 |
| NO 2006000655 | A | 20060616 | NO 2006-655 | 20060209 |
| PRIORITY APPLN. INFO.: | | | US 2003-504508P | P 20030919 |

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WO 2004-IB2912

W 20040906

OTHER SOURCE(S): MARPAT 142:310354

IT 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

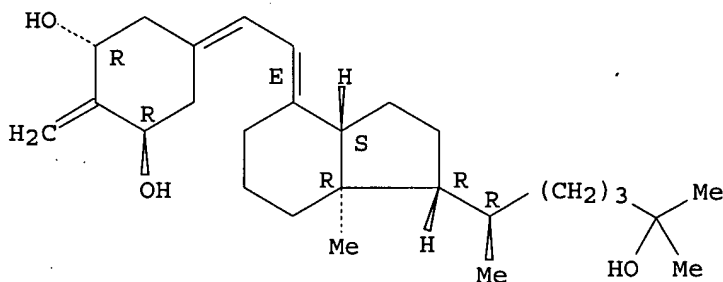
(preparation of 2-alkylidene-19-nor-vitamin D derivs. for treatment of osteopenia or male osteoporosis)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



AB The present invention relates to methods of treating osteopenia or male osteoporosis, the methods comprising administering to a patient in need thereof a 2-alkylidene-19-nor-vitamin D derivative. Particularly, the present invention relates to methods of treating osteopenia or male osteoporosis, the methods comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D 3.

L10 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259654 CAPLUS

DOCUMENT NUMBER: 142:291906

TITLE: Use of 2-methylene-19-nor-20(s)-1 α ,25-dihydroxyvitamin D3 to increase the life expectancy of human beings

INVENTOR(S): DeLuca, Hector F.; Plum, Lori A.; Clagette-Dame, Margaret

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 5 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2005065123 | A1 | 20050324 | US 2003-669990 | 20030924 |
| AU 2004280176 | A1 | 20050421 | AU 2004-280176 | 20040728 |
| CA 2540051 | A1 | 20050421 | CA 2004-2540051 | 20040728 |
| WO 2005034959 | A1 | 20050421 | WO 2004-US24482 | 20040728 |

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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1663251 A1 20060607 EP 2004-757375 20040728

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

US 2006241090 A1 20061026 US 2006-472125 20060621

PRIORITY APPLN. INFO.: US 2003-669990 A 20030924

WO 2004-US24482 W 20040728

IT 213250-70-5, 2-Methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin

D3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

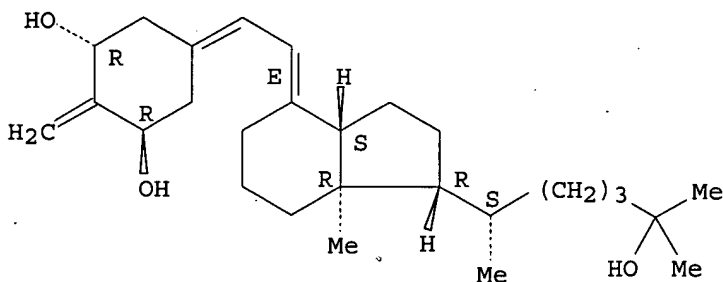
(method for increasing the life expectancy of human beings)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D3. Administration of this compound increases the life expectancy of human beings, especially elderly human beings. In particular, it increases the survival rate of females lacking estrogen, especially post-menopausal females, and reduces mortality resulting from spontaneous development of malignant tumors in both males and females.

L10 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259653 CAPLUS

DOCUMENT NUMBER: 142:317003

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a bisphosphonate

INVENTOR(S): Lee, Andrew G.

PATENT ASSIGNEE(S): Pfizer Inc, USA

SOURCE: U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

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|---------------|----|----------|-----------------|----------|
| US 2005065117 | A1 | 20050324 | US 2004-942426 | 20040916 |
| AU 2004273672 | A1 | 20050331 | AU 2004-273672 | 20040906 |
| CA 2539359 | A1 | 20050331 | CA 2004-2539359 | 20040906 |
| WO 2005027921 | A1 | 20050331 | WO 2004-IB2935 | 20040906 |

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
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| EP 1667691 | A1 | 20060614 | EP 2004-769333 | 20040906 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |

| | | | | |
|---------------|---|----------|------------------|----------|
| CN 1852719 | A | 20061025 | CN 2004-80027165 | 20040906 |
| BR 2004014565 | A | 20061107 | BR 2004-14565 | 20040906 |
| NO 2006001245 | A | 20060531 | NO 2006-1245 | 20060317 |

| | | | |
|------------------------|-----------------|---|----------|
| PRIORITY APPLN. INFO.: | US 2003-504008P | P | 20030919 |
| | WO 2004-IB2935 | W | 20040906 |

IT 213250-70-5P 213319-29-0P

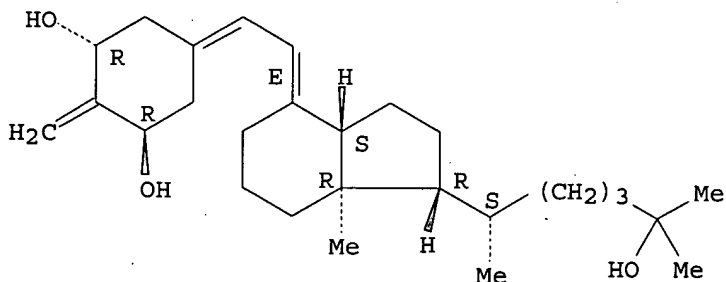
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and aromatase inhibitors)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

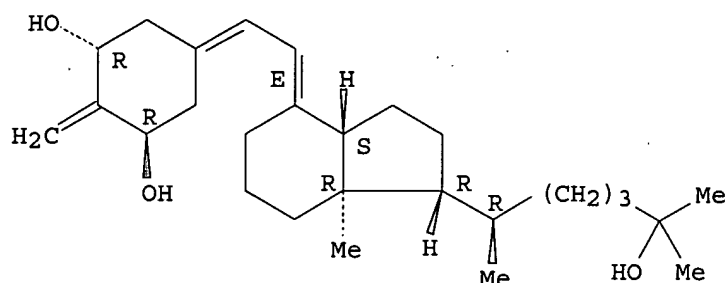


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and a bisphosphonate. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D3 and a bisphosphonate.

L10 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259643 CAPLUS

DOCUMENT NUMBER: 142:317002

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin d derivatives and parathyroid hormone

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| US 2005065088 | A1 | 20050324 | US 2004-946585 | 20040916 |
| AU 2004273660 | A1 | 20050331 | AU 2004-273660 | 20040906 |
| CA 2539357 | A1 | 20050331 | CA 2004-2539357 | 20040906 |
| WO 2005027915 | A1 | 20050331 | WO 2004-IB2902 | 20040906 |
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| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1667689 | A1 | 20060614 | EP 2004-769301 | 20040906 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| CN 1852716 | A | 20061025 | CN 2004-80026848 | 20040906 |
| BR 2004014518 | A | 20061107 | BR 2004-14518 | 20040906 |
| NO 2006001236 | A | 20060615 | NO 2006-1236 | 20060317 |
| PRIORITY APPLN. INFO.: | | | US 2003-504503P | P 20030919 |

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WO 2004-IB2902

W 20040906

OTHER SOURCE(S): CASREACT 142:317002

IT 213250-70-5P 213319-29-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

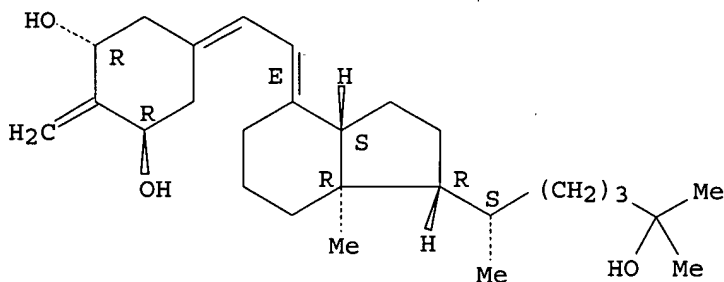
(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and parathyroid hormone)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

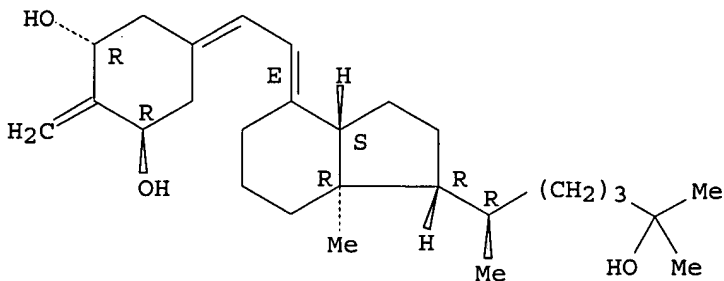


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and parathyroid hormone or an active fragment or variant thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D3 and parathyroid hormone or an active fragment or variant thereof.

L10 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259642 CAPLUS

DOCUMENT NUMBER: 142:317001

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D

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INVENTOR(S): derivatives and a bone morphogenetic protein
Campagnari, Judith L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2005065087 | A1 | 20050324 | US 2004-942725 | 20040916 |
| WO 2005027926 | A1 | 20050331 | WO 2004-IB2905 | 20040906 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2003-504161P P 20030919

IT 213250-70-5P 213319-29-0P

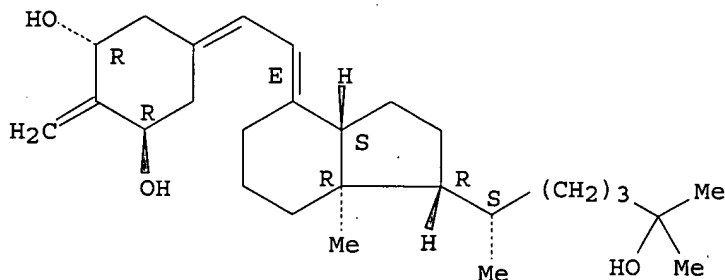
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivs. and bone morphogenetic protein)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

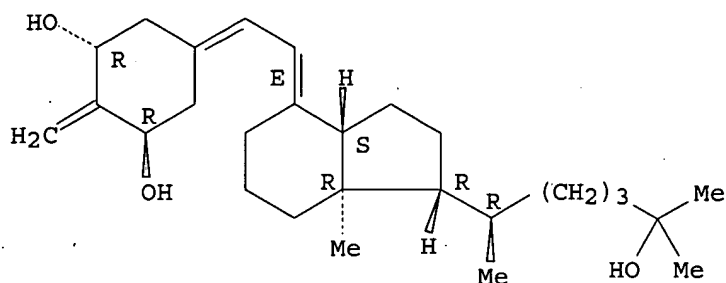


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivs. and a bone morphogenetic protein or active fragment or variant thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D 3 and a bone morphogenetic protein or active fragment or variant thereof.

L10 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:259356 CAPLUS

DOCUMENT NUMBER: 142:322752

TITLE: Pharmaceutical compositions and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and an estrogen

INVENTOR(S): Keys, Sharon C.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| US 2005063992 | A1 | 20050324 | US 2004-942384 | 20040916 |
| WO 2005027929 | A1 | 20050331 | WO 2004-IB2911 | 20040906 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2003-504023P P 20030919

IT 213250-70-5P 213319-29-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(compns. comprising alkylidene vitamin D derivs. in combination with estrogen for treatment of bone disease, cancer and other diseases)

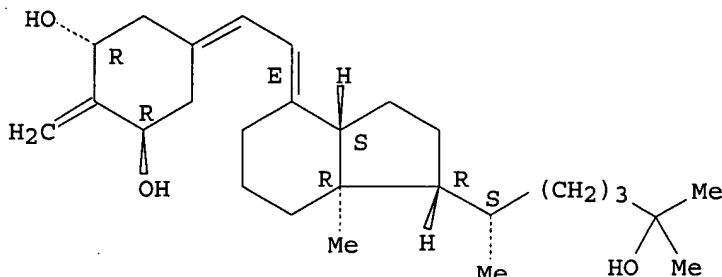
RN 213250-70-5 CAPLUS

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CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

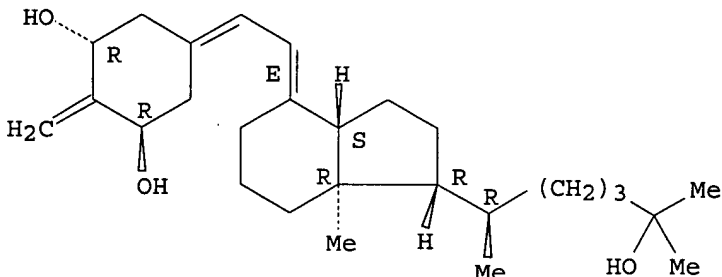
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB The present invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need thereof a combination of a 2-alkylidene-19-nor-vitamin D derivative and an estrogen, or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the present invention relates to pharmaceutical compns. and methods of treatment, e.g. osteoporosis, bone fracture, breast cancer, prostate cancer, obesity, osteopenia, etc., comprising administering to a patient in need thereof 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃ (I) and an estrogen, or a pharmaceutically acceptable salt or prodrug thereof. For example, I was prepared and tested for biol. activity. I bound well to the porcine intestinal vitamin D receptor. When given at 130 pmol/day, its activity on bone calcium mobilization (serum calcium) was of the order of at least 10 and possible 100 to 1000 times more than that of the native hormone. Also, I was extremely potent in inducing differentiation of HL-60 cells to monocyte, illustrating its potential as anticancer agent.

L10 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:522177 CAPLUS

DOCUMENT NUMBER: 141:185224

TITLE: Model of three-dimensional structure of VDR bound with Vitamin D₃ analogs substituted at carbon-2

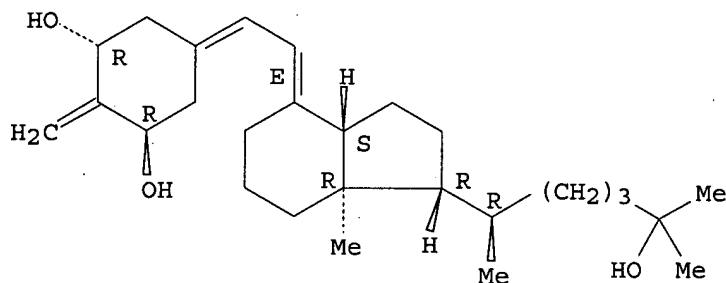
AUTHOR(S): Sicinska, Wanda; Rotkiewicz, Piotr; DeLuca, Hector F.

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CORPORATE SOURCE: Department of Biochemistry, University of
Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Steroid Biochemistry and Molecular Biology
(2004), 89-90(1-5), 107-110
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: : Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213319-29-0
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(model of three-dimensional structure of VDR bound with Vitamin D3
analogs substituted at carbon-2)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB All Vitamin D analogs possessing the A ring modified at C-2 and showing calcemic activities nest themselves in the VDR binding pocket, oriented towards Tyr 143. Such topol. resembles the position of the Vitamin D hormone in hVDRmt [Proc. Natl. Acad. Sci. U.S.A. 98 (2001) 5491]. Conversely, inactive 2 β -methyl-19-nor-analogs anchor the receptor cavity in a distinguishably different manner, namely by their side chain. Moreover, these inactive vitamins have a different conformation around C(6)-C(7) bond. Topol. of modeled complexes suggests that a Vitamin D analog will be biol. active if its intercylic 5,7-diene moiety assumes parallel position to tryptophan aromatic rings; such orientation allows for creating π - π interactions. The broad comparison of calcemic activities of the analogs, and their interactions with VDR, revealed that specific hydrophobic contacts are involved in bone calcium mobilization (BCM). These contacts occur between 21-Me group and a few amino acids (V296, L305 and L309), conserved in the nuclear receptor superfamily. In the inactive 2 β -methyl-19-nor analogs such contacts do not exist. We speculate that two hydrophobic receptor patches, being in close contact with ligand Me groups, might influence interaction with co-modulators involved in calcium homeostasis.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

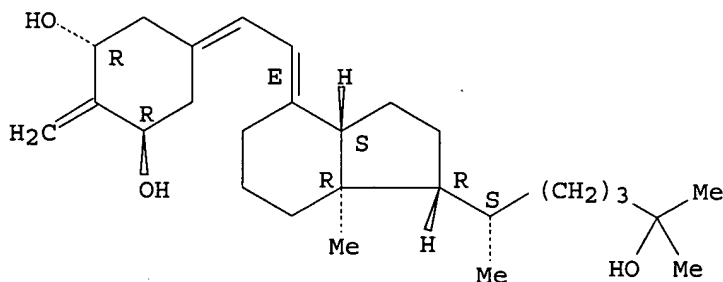
L10 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:522171 CAPLUS
DOCUMENT NUMBER: 141:185221
TITLE: Therapeutic potential of the 2-alkyl and
2-alkylidene-19-nor-(20S)-modified analogs of
1 α ,25-dihydroxyvitamin D3

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AUTHOR(S): DeLuca, Hector F.
CORPORATE SOURCE: Department of Biochemistry, University of
Wisconsin-Madison, Madison, WI, 53706-1544, USA
SOURCE: Journal of Steroid Biochemistry and Molecular Biology
(2004), 89-90(1-5), 67-73
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: : Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213250-70-5
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of 2-alkyl and 2-alkylidene-19-nor-(20S)-modified analogs of
1 α ,25-(OH)2D3 on PTH activity/bone mineral mobilization, and
their therapeutic potential for diseases where a rise in serum calcium
is not desired)
RN 213250-70-5 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Five analogs of 19-nor-1 α ,25-dihydroxyvitamin D3 are described that show highly selective and potent activities. The 2-methylene-19-nor-(20S)-1 α ,25-dihydroxyvitamin D3 (2MD) and its 2 α -Me sister are selectively active on the osteoblast. 2MD is bone anabolic and causes bone formation in vivo and in vitro and is being developed as a therapy for bone loss diseases such as osteoporosis. 2-Methylene-19-nor-(20S)-bishomo-1 α -hydroxypregnacalciferol (2BMP) has no activity on calcium in vivo while totally suppressing circulating parathyroid hormone. Its homologs, i.e. 2-methylene-19-nor-1 α -hydroxy-homopregnacalciferol (2MP) and 2-methylene-19-nor-1 α -hydroxypregnacalciferol (2MPC) act similarly but are either less selective (2MP) or not as potent (2MPC). These abbreviated side chain analogs will be developed for diseases where a rise in serum calcium is not desired, as for example, cancer, renal osteodystrophy, psoriasis and autoimmune diseases.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:220021 CAPLUS

DOCUMENT NUMBER: 140:247113

TITLE: Method of extending the dose range of vitamin D compounds

INVENTOR(S): DeLuca, Hector F.; Pike, John W.; Shevde, Nirupama;
Plum, Lori A.; Clagett-Dame, Margaret

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PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| US 2004053813 | A1 | 20040318 | US 2002-235244 | 20020905 |
| CA 2497828 | A1 | 20040318 | CA 2003-2497828 | 20030626 |
| WO 2004022068 | A1 | 20040318 | WO 2003-US20517 | 20030626 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003245748 | A1 | 20040329 | AU 2003-245748 | 20030626 |
| EP 1545549 | A1 | 20050629 | EP 2003-739354 | 20030626 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003014006 | A | 20050809 | BR 2003-14006 | 20030626 |
| CN 1694711 | A | 20051109 | CN 2003-824888 | 20030626 |
| JP 2006500388 | T | 20060105 | JP 2004-534233 | 20030626 |
| PRIORITY APPLN. INFO.: | | | US 2002-235244 | A 20020905 |
| | | | WO 2003-US20517 | W 20030626 |

OTHER SOURCE(S): MARPAT 140:247113

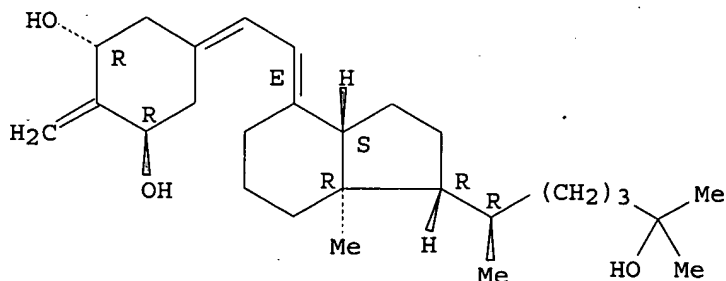
IT 213319-29-0

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method of extending dose range of vitamin D compds.)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Inhibitors of bone calcium resorption are administered to allow high doses of vitamin D compds. or mimetics (Markush structures are given) to be given with the intent of treating non-calcium related diseases such as cancer, psoriasis, and autoimmune disease without the dangers of

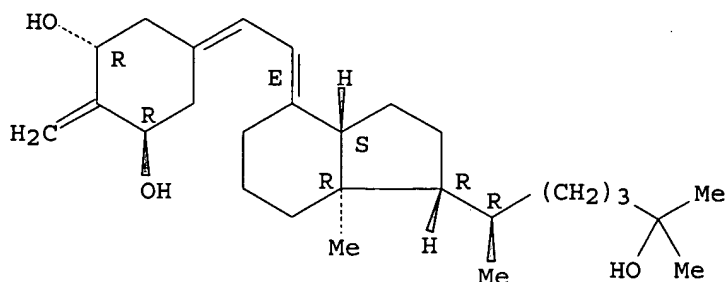
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calcification of kidney, heart, and aorta. Inhibitors of bone calcium resorption include the bis-phosphonates, OPG or the soluble RANKL receptor known as sRANK, and function to block the availability of calcium from bone thereby preventing hypercalcemia and the resulting calcification of soft tissues. Thus, high doses of $1\alpha,25$ -dihydroxyvitamin D₃ ($1,25$ -(OH)₂D₃), its analogs, prodrugs, or mimetics can be utilized with minimal risk to a patient. Specifically, alendronate is shown to block the bone calcium mobilization activity of both $1,25$ -(OH)₂D₃ and its very potent analog, 2-methylene-19-nor-20(S)- $1\alpha,25$ -dihydroxyvitamin D₃.

L10 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:647469 CAPLUS
DOCUMENT NUMBER: 139:271426
TITLE: 2-Methylene-19-nor-(20S)- $1,25$ -dihydroxyvitamin D₃
potently stimulates gene-specific DNA binding of
vitamin D receptor in osteoblasts
AUTHOR(S): Yamamoto, Hironori; Shevde, Nirupama K.; Warrier,
Anjali; Plum, Lori A.; DeLuca, Hector F.; Pike, J.
Wesley
CORPORATE SOURCE: Department of Biochemistry, University of
Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Biological Chemistry (2003), 278(34),
31756-31765
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 213319-29-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2-methylene-19-nor-(20S)- $1,25$ -dihydroxyvitamin D₃ potently stimulates
gene-specific DNA binding of vitamin D receptor in osteoblasts in
relation to underlying mol. mechanism)
RN 213319-29-0 CAPLUS
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
($1\alpha,3\beta,7E$)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB 2-Methylene-19-nor-(20S)- $1,25$ -dihydroxyvitamin D₃ (2MD) is a highly potent analog of $1,25$ -dihydroxyvitamin D₃ ($1,25$ (OH)₂D₃) whose actions are mediated through the vitamin D receptor (VDR). The authors have replicated this increased potency of 2MD in vitro using osteoblastic cells and explored its underlying mol. mechanism. 2MD stimulates the expression of several vitamin D-sensitive genes including 25 -hydroxyvitamin D₃-24 hydroxylase (Cyp24), osteopontin and receptor activator of NF κ B

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ligand and suppresses osteoprotegerin at concns. two logs lower than that for 1,25(OH)2D3. 2MD is also more potent in stimulating transfected chimeric reporter genes under either Cyp24 or the osteocalcin promoter control. Enhanced potency is retained regardless of medium serum content. Interestingly, the uptake of both 1,25(OH)2D3 and 2MD into cells is similar, as is their rapid association with the VDR. This indicates that comparable levels of occupied VDR do not elicit equivalent levels of transactivation. Using chromatin immunopptn. (ChIP), however, the authors observed a strong correlation between DNA-bound receptor and the level of induced transcription suggesting a 2MD-induced increase in affinity of the VDR for DNA. Addnl. studies using a mammalian two-hybrid system and ChIP indicate that 2MD is also more potent in promoting interaction with RXR and the coactivators SRC-1 and DRIP205. Finally, protease digestion studies revealed a unique VDR conformation in the presence of 2MD. These studies suggest that the mol. mechanism of 2MD potency is due to its ability to promote enhanced levels of specific DNA binding by the VDR and could suggest possible explanations for the tissue- and gene-selective actions of 2MD.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:387626 CAPLUS
DOCUMENT NUMBER: 136:401925
TITLE: Preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 370,966, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 6392071 | B1 | 20020521 | US 2000-540686 | 20000331 |
| US 5843928 | A | 19981201 | US 1997-819693 | 19970317 |
| US 5936133 | A | 19990810 | US 1998-151113 | 19980910 |
| CA 2404548 | A1 | 20011011 | CA 2001-2404548 | 20010329 |
| WO 2001074766 | A1 | 20011011 | WO 2001-US10317 | 20010329 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1268416 | A1 | 20030102 | EP 2001-920897 | 20010329 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003529581 | T | 20031007 | JP 2001-572461 | 20010329 |
| NZ 522160 | A | 20041126 | NZ 2001-522160 | 20010329 |
| US 2002087015 | A1 | 20020704 | US 2001-1711 | 20011031 |
| US 6537981 | B2 | 20030325 | | |

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| | | | | |
|------------------------|----|----------|-----------------|-------------|
| US 2003181427 | A1 | 20030925 | US 2003-352745 | 20030128 |
| US 6696431 | B2 | 20040224 | | |
| US 2004167104 | A1 | 20040826 | US 2004-780103 | 20040217 |
| US 7094774 | B2 | 20060822 | | |
| JP 2006117680 | A | 20060511 | JP 2005-319365 | 20051102 |
| PRIORITY APPLN. INFO.: | | | US 1997-819693 | A3 19970317 |
| | | | US 1998-151113 | A1 19980910 |
| | | | US 1999-370966 | B2 19990810 |
| | | | JP 1998-540501 | A3 19980211 |
| | | | US 2000-540686 | A 20000331 |
| | | | WO 2001-US10317 | W 20010329 |
| | | | US 2001-1711 | A3 20011031 |
| | | | US 2003-352745 | A3 20030128 |

OTHER SOURCE(S): MARPAT 136:401925

IT 213250-70-5P 213319-29-0P

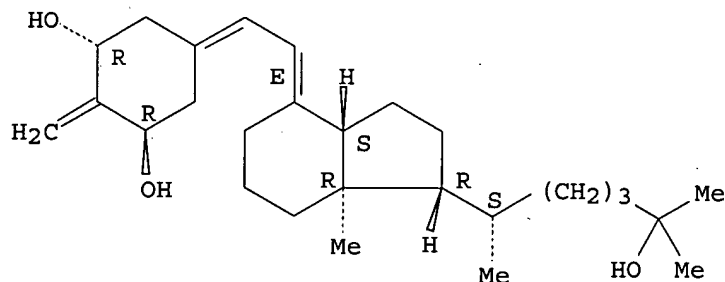
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 26,27-homologated-20-epi-2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

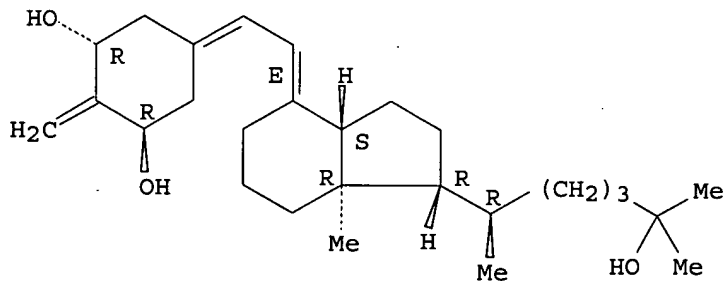
Absolute stereochemistry.
Double bond geometry as shown.



RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R6, R8 = alkyl, hydroxyalkyl, fluoroalkyl, etc., or when taken together represent the group -(CH2)x- where x is an integer from 2 to 5; R = any of the typical side chains known for vitamin D type compds.] are prepared These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. Thus, 20(S)-1 α ,25-dihydroxy-2-methylene-26,27-dihomo-19-nor-vitamin D3 (II) was prepared via a multistep synthetic sequence starting from 20(S)-25-hydroxy Grundmann's ketone analog III and phosphine oxide IV. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in vitamin D-deficient rats on a low calcium diet responding to chronic doses of II at 15 pmol/day/7 days were 4.0 \pm 0.4 S/M and 5.3 \pm 0.1 S/M resp. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:332679 CAPLUS

DOCUMENT NUMBER: 136:335278

TITLE: 1 α -Hydroxy-2-methylene-19-nor-homopregnacalciferol and its therapeutic uses

INVENTOR(S): DeLuca, Hector F.; Sicinski, Rafal R.; Gowlugari, Sumithra; Plum, Lori A.; Clagett-Dame, Margaret

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U. S. Ser. No. 657,828.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2002052350 | A1 | 20020502 | US 2001-878438 | 20010611 |
| US 6440953 | B2 | 20020827 | | |
| PT 1315504 | T | 20041231 | PT 2001-942154 | 20010611 |
| ES 2227215 | T3 | 20050401 | ES 2001-1942154 | 20010611 |
| US 2002183289 | A1 | 20021205 | US 2002-165123 | 20020607 |
| US 6579861 | B2 | 20030617 | | |

PRIORITY APPLN. INFO.: US 2000-657828 A2 20000908
US 2001-878438 A3 20010611

IT 213250-70-5

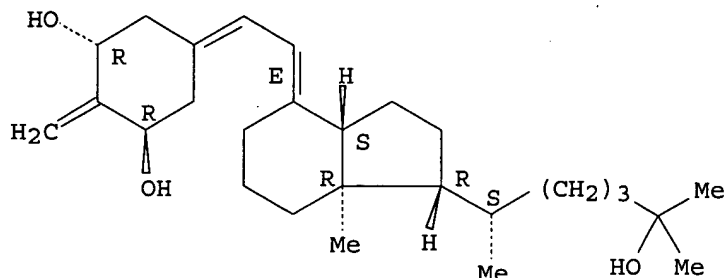
RL: PAC (Pharmacological activity); BIOL (Biological study)
(hydroxymethylenenorhomopregnacalciferol and therapeutic use)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

QAZI

Absolute stereochemistry.
Double bond geometry as shown.



AB The invention discloses 1 α -hydroxy-2-methylene-19-nor-homopregnacalciferol and its pharmaceutical uses. This compound exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as an anti-cancer agent and for the treatment of skin diseases such as psoriasis as well as skin conditions such as wrinkles, slack skin, dry skin and insufficient sebum secretion. This compound also has little, if any, calcemic activity and therefore may be used to treat immune disorders in humans as well as renal osteodystrophy.

L10 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:71881 CAPLUS

DOCUMENT NUMBER: 136:112696

TITLE: Use of 2-methylene-19-nor-20(S)-1 α ,25-dihydroxyvitamin D₃ to increase bone strength and for the treatment of skin disease, cancer, and bone disease

INVENTOR(S): Deluca, Hector F.; Smith, Connie M.

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002005823 | A2 | 20020124 | WO 2001-US21706 | 20010710 |
| WO 2002005823 | A3 | 20020523 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2416194 | A1 | 20020124 | CA 2001-2416194 | 20010710 |
| AU 2001078888 | A5 | 20020130 | AU 2001-78888 | 20010710 |
| EP 1301189 | A2 | 20030416 | EP 2001-957115 | 20010710 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |

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|---------------|----|----------|----------------|----------|
| BR 2001012454 | A | 20030729 | BR 2001-12454 | 20010710 |
| JP 2004505022 | T | 20040219 | JP 2002-511755 | 20010710 |
| NZ 537036 | A | 20060728 | NZ 2001-537036 | 20010710 |
| US 2004068129 | A1 | 20040408 | US 2003-673629 | 20030929 |
| US 7115594 | B2 | 20061003 | | |
| HK 1060304 | A1 | 20060421 | HK 2004-103322 | 20040512 |
| US 2006135492 | A1 | 20060622 | US 2006-350554 | 20060209 |
| US 2006135493 | A1 | 20060622 | US 2006-350555 | 20060209 |

PRIORITY APPLN. INFO.:

| | | |
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| US 2000-616164 | A | 20000714 |
| WO 2001-US21706 | W | 20010710 |
| US 2003-673629 | A3 | 20030929 |

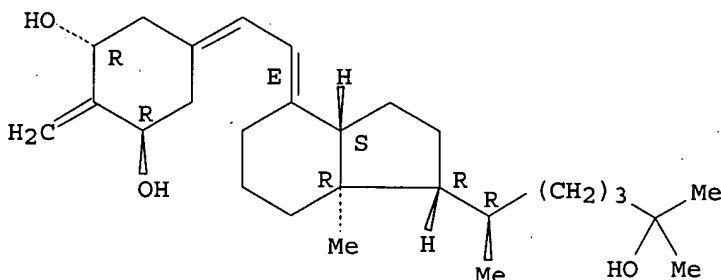
IT 213319-29-0

RL: PAC (Pharmacological activity); BIOL (Biological study)
 (methylenenordihydroxyvitamin D3 to increase bone strength and for
 treatment of skin disease, cancer, and bone disease)

RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
 (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



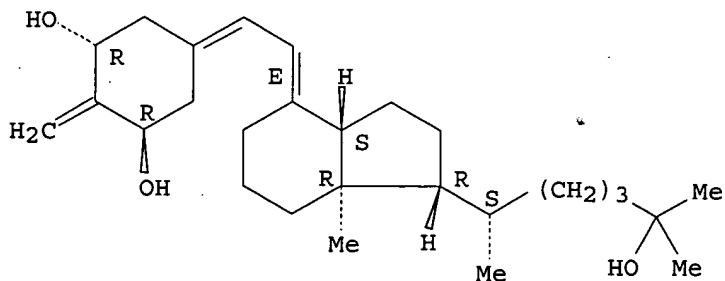
IT 213250-70-5

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (methylenenordihydroxyvitamin D3 to increase bone strength and for
 treatment of skin disease, cancer, and bone disease)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
 (1 α ,3 β ,7E,20S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



AB The invention provides pharmaceutical uses for 2-methylene-19-nor-20(S)-
 1 α ,25-dihydroxyvitamin D3. This compound is characterized by high

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bone calcium mobilization activity demonstrating preferential activity on bone. This results in a novel therapeutic agent for the treatment of diseases where bone formation is desired, particularly osteoporosis. This compound also exhibits pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte, thus evidencing use as an anticancer agent and for the treatment of skin diseases such as psoriasis. This compound also increases both breaking strength and crushing strength of bones evidencing use in conjunction with bone replacement surgery such as hip and knee replacements.

L10 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:830900 CAPLUS

DOCUMENT NUMBER: 135:358086

TITLE: Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compounds

INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 454,013.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| US 6316642 | B1 | 20011113 | US 2000-541470 | 20000331 |
| US 5945410 | A | 19990831 | US 1997-819694 | 19970317 |
| US 6127559 | A | 20001003 | US 1998-135463 | 19980817 |
| US 6277837 | B1 | 20010821 | US 1999-454013 | 19991203 |
| CA 2403232 | A1 | 20011011 | CA 2001-2403232 | 20010329 |
| WO 2001074765 | A1 | 20011011 | WO 2001-US10094 | 20010329 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1268415 | A1 | 20030102 | EP 2001-920863 | 20010329 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004500414 | T | 20040108 | JP 2001-572460 | 20010329 |
| NZ 521236 | A | 20051028 | NZ 2001-521236 | 20010329 |
| US 2002123638 | A1 | 20020905 | US 2001-999299 | 20011031 |
| US 6544969 | B2 | 20030408 | | |
| US 2003073857 | A1 | 20030417 | US 2002-246968 | 20020919 |
| US 6667298 | B2 | 20031223 | | |
| US 2004072804 | A1 | 20040415 | US 2003-673618 | 20030929 |
| US 6939868 | B2 | 20050906 | | |
| US 2004082802 | A1 | 20040429 | US 2003-683330 | 20031010 |
| US 7112579 | B2 | 20060926 | | |
| JP 2006096759 | A | 20060413 | JP 2005-319359 | 20051102 |
| PRIORITY APPLN. INFO.: | | | US 1997-819694 | A2 19970317 |
| | | | US 1998-135463 | A3 19980817 |
| | | | US 1999-454013 | A2 19991203 |
| | | | JP 1998-540500 | A3 19980211 |
| | | | US 2000-541470 | A 20000331 |

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|-----------------|-------------|
| WO 2001-US10094 | W 20010329 |
| US 2001-45941 | B3 20011019 |
| US 2001-999299 | A3 20011031 |
| US 2002-246968 | A3 20020919 |

OTHER SOURCE(S): MARPAT 135:358086

IT 213319-29-0P

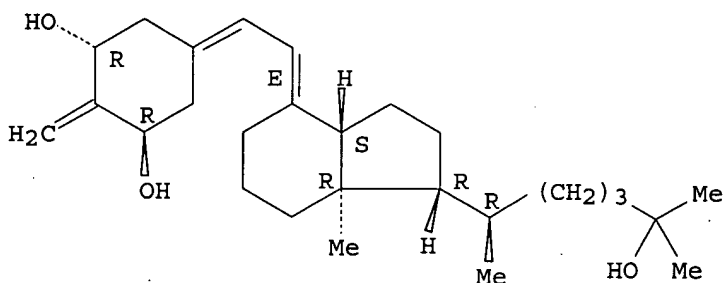
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 26,27-homologated-20-epi-2-alkyl-19-norvitamin D compds. with high intestinal calcium transport activity)

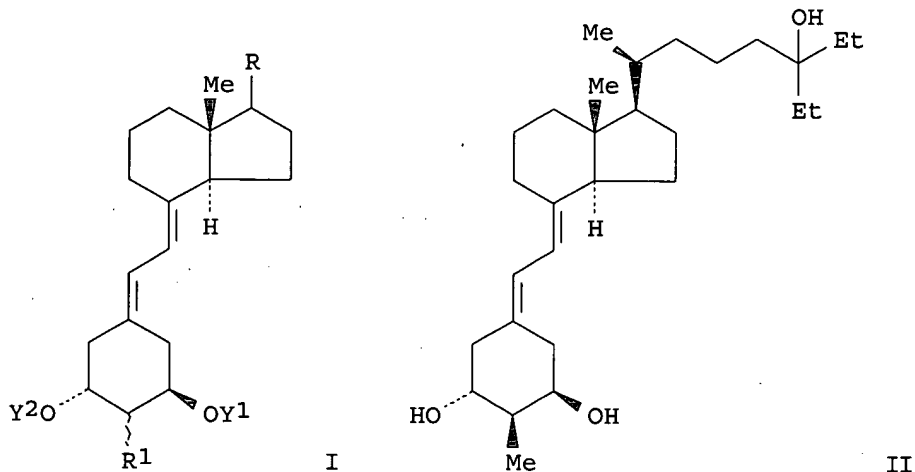
RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [Y1, Y2 = H, protecting group; R = typical side chains known for vitamin D type compds.; R1 = alkyl, hydroxyalkyl, fluoroalkyl] are prepared These 2-substituted compds., especially the 2 α -Me and the 2 α -methyl-20S derivs., are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel

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therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II was prepared and showed preferential activity on bone in biol. activity tests.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:747743 CAPLUS

DOCUMENT NUMBER: 135:288953

TITLE: Preparation of 2-alkylidene-19-nor-vitamin D compounds as antiosteoporotics and antitumor agents

INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2001074766 | A1 | 20011011 | WO 2001-US10317 | 20010329 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 6392071 | B1 | 20020521 | US 2000-540686 | 20000331 |
| CA 2404548 | A1 | 20011011 | CA 2001-2404548 | 20010329 |
| EP 1268416 | A1 | 20030102 | EP 2001-920897 | 20010329 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2003529581 | T | 20031007 | JP 2001-572461 | 20010329 |
| NZ 522160 | A | 20041126 | NZ 2001-522160 | 20010329 |
| PRIORITY APPLN. INFO.: | | | US 2000-540686 | A 20000331 |
| | | | US 1997-819693 | A3 19970317 |
| | | | US 1998-151113 | A1 19980910 |
| | | | US 1999-370966 | B2 19990810 |
| | | | WO 2001-US10317 | W 20010329 |

OTHER SOURCE(S): MARPAT 135:288953

IT 213319-29-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-alkylidene-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

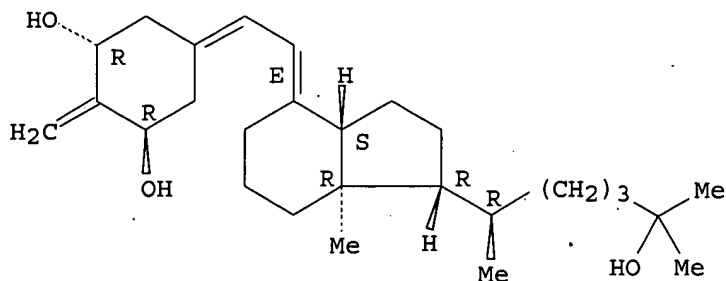
RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

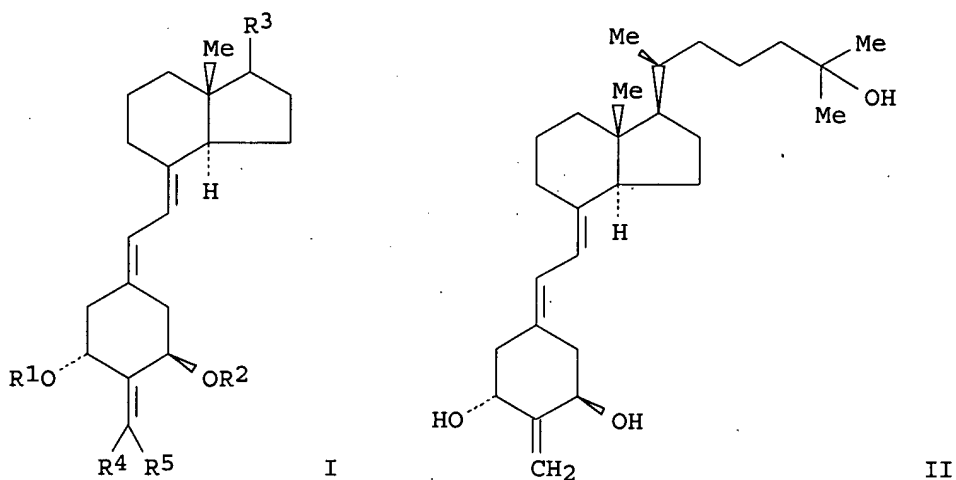
Absolute stereochemistry.

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Double bond geometry as shown.



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AB Novel vitamin D related compds., namely, 2-alkylidene-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = typical side chains known for vitamin D type compds.; R4, R5 = H, alkyl, hydroxyalkyl, fluoroalkyl, etc.; R4R5 = cycloalkylidene] are prepared. These 2-substituted compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anticancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and is found to be extremely potent in inducing differentiation of HL-60 cells.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:747742 CAPLUS
DOCUMENT NUMBER: 135:304063
TITLE: Preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-
vitamin D compounds

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INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2001074765 | A1 | 20011011 | WO 2001-US10094 | 20010329 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 6316642 | B1 | 20011113 | US 2000-541470 | 20000331 |
| CA 2403232 | A1 | 20011011 | CA 2001-2403232 | 20010329 |
| EP 1268415 | A1 | 20030102 | EP 2001-920863 | 20010329 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| JP 2004500414 | T | 20040108 | JP 2001-572460 | 20010329 |
| NZ 521236 | A | 20051028 | NZ 2001-521236 | 20010329 |
| US 2004072804 | A1 | 20040415 | US 2003-673618 | 20030929 |
| US 6939868 | B2 | 20050906 | | |
| PRIORITY APPLN. INFO.: | | | US 2000-541470 | A 20000331 |
| | | | US 1997-819694 | A2 19970317 |
| | | | US 1998-135463 | A3 19980817 |
| | | | US 1999-454013 | A2 19991203 |
| | | | WO 2001-US10094 | W 20010329 |
| | | | US 2001-45941 | B3 20011019 |

OTHER SOURCE(S): MARPAT 135:304063

IT 213250-70-5P 213319-29-0P

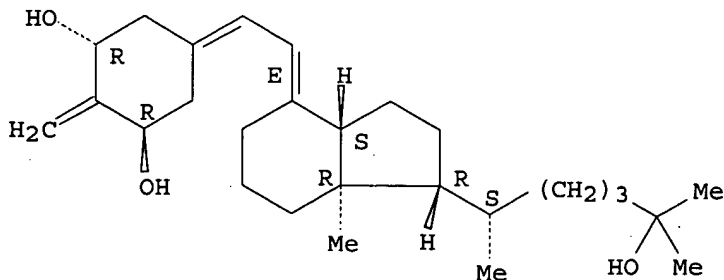
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 26,27-homologated-20-epi-2-alkyl-19-nor-vitamin D compds. as antiosteoporotics and antitumor agents)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



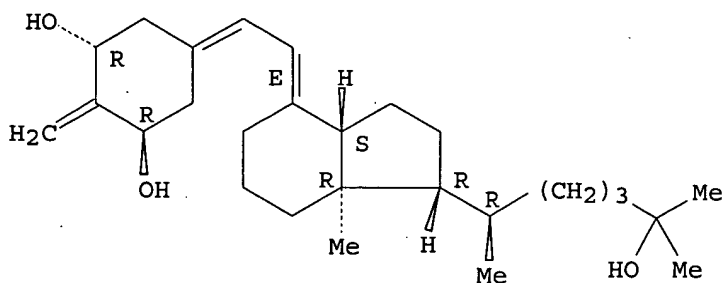
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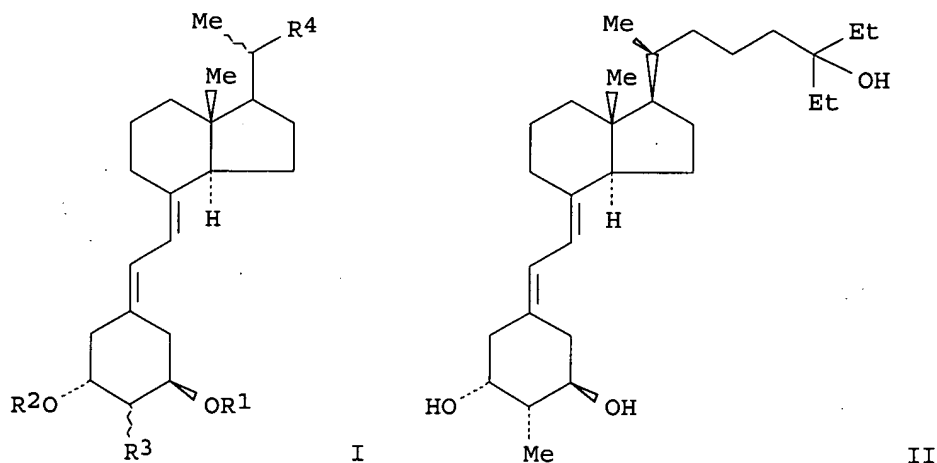
RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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AB 2-Alkyl-19-nor-vitamin D derivs. of formula I [R1, R2 = H, protecting group; R3 = alkyl, hydroxyalkyl, fluoroalkyl; R4 = H, Me, acyl, OH, any of the typical side chains known for vitamin D type compds., etc.] are prepared. These compds. are characterized by relatively high intestinal calcium transport activity and relatively high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis. Thus, II is prepared and had a VDR binding ratio of 5.5, and HL-60 differentiation ED50 of 1.1 x 10⁻¹⁰ M.

REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L10 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:699222 CAPLUS
DOCUMENT NUMBER: 133:267021
TITLE: preparation and therapeutic use of
2-alkyl-19-nor-vitamin D derivatives
INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. 5,945,410.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 6127559 | A | 20001003 | US 1998-135463 | 19980817 |
| US 5945410 | A | 19990831 | US 1997-819694 | 19970317 |
| PT 971888 | T | 20040331 | PT 1998-905101 | 19980211 |
| ES 2206893 | T3 | 20040516 | ES 1998-905101 | 19980211 |
| US 6277837 | B1 | 20010821 | US 1999-454013 | 19991203 |
| US 6316642 | B1 | 20011113 | US 2000-541470 | 20000331 |
| US 6306844 | B1 | 20011023 | US 2000-616778 | 20000714 |
| US 2002151528 | A1 | 20021017 | US 2001-45941 | 20011019 |
| US 2002123638 | A1 | 20020905 | US 2001-999299 | 20011031 |
| US 6544969 | B2 | 20030408 | | |
| US 2003073857 | A1 | 20030417 | US 2002-246968 | 20020919 |
| US 6667298 | B2 | 20031223 | | |
| US 2004072804 | A1 | 20040415 | US 2003-673618 | 20030929 |
| US 6939868 | B2 | 20050906 | | |
| US 2004082802 | A1 | 20040429 | US 2003-683330 | 20031010 |
| US 7112579 | B2 | 20060926 | | |
| US 2006003973 | A1 | 20060105 | US 2005-216951 | 20050831 |
| JP 2006096759 | A | 20060413 | JP 2005-319359 | 20051102 |

PRIORITY APPLN. INFO.:

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| US 1997-819694 | A2 | 19970317 |
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| US 2000-616778 | A3 | 20000714 |
| JP 2001-83085 | A | 20010322 |
| US 2001-45941 | B3 | 20011019 |
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| US 2002-246968 | A3 | 20020919 |
| US 2003-673618 | A3 | 20030929 |

OTHER SOURCE(S): MARPAT 133:267021

IT 213250-70-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

RN 213250-70-5 CAPLUS

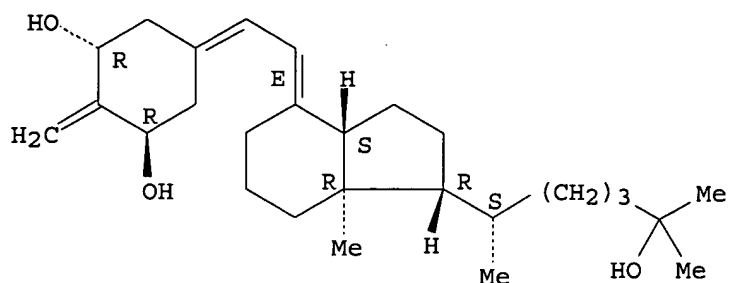
CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

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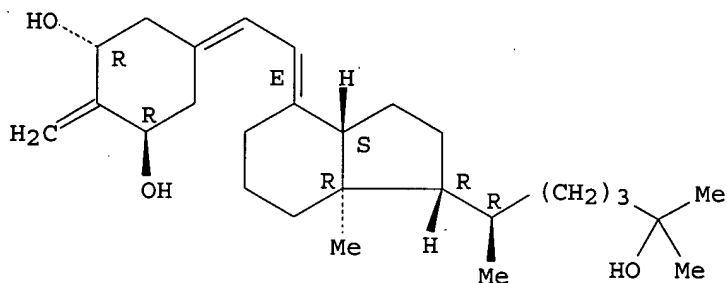
IT 213319-29-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation and therapeutic use of 2-alkyl-19-nor-vitamin D analog)

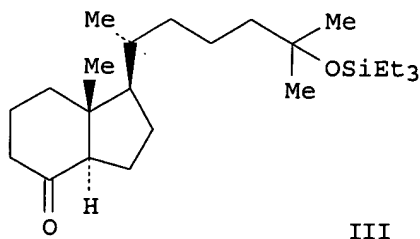
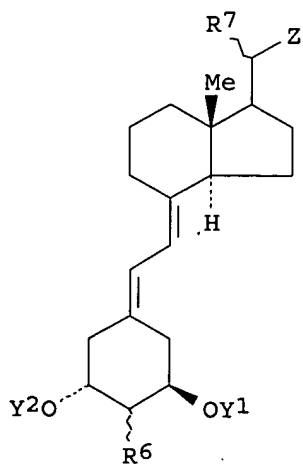
RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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AB This invention discloses a novel class of vitamin D related compds., namely, the 2-alkyl-19-nor-vitamin D derivs. (I) ($Y_1, Y_2 = H$, hydroxy-protecting group; $R_6 = \text{alkyl, hydroxyalkyl, fluoroalkyl}$; $R_7 = \alpha \text{ or } \beta\text{-Me}$; $Z = Y, -OY, -CH_2OY, -C.tplbond.CY, -CH=CHY$ ($Y = H, Me, -(CH_2)_m-C(R_1R_2)-(CH_2)_n-C(R_3R_4R_5)$; where m and n , independently integers from 0-5; $R_1 = H, OH, \text{protected hydroxy, F, CF}_3, \text{alkyl etc.}$, $R_2, R_3, R_4 = D, \text{deuteroalkyl, H, F, CF}_3, \text{alkyl etc.}$, $R_1+R_2 = O, =C(R_2R_3) \text{ etc.}$, $R_5 = H, OH, \text{protected hydroxy, alkyl, and wherein any of the CH-groups at position 20, 22, or 23 in the side chain may be replaced by a N atom or where any of the groups } -CH(Me)-, -CH(R_3)-, \text{ or } -CH(R_2)- \text{ at positions 20, 22, and 23, resp., may be replaced by an oxygen or sulfur atom})$), were prepared Thus, I ($Y_1, Y_2 = H$; $R_6, R_7 = \alpha\text{-Me}$; $Z = (CH_2)_3C(Me)_2OH$) (II) was prepared starting from Me quinate and followed by Wittig-Horner coupling with Grundman's ketone (III). The 2-substituted compds., especially the 2 α -Me and the 2 α -methyl-20S derivs., are characterized by relatively low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. I also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:505692 CAPLUS

DOCUMENT NUMBER: 131:144749

TITLE: Preparation of 14-epi-19-nor-vitamin D compounds with cell differentiation activity

INVENTOR(S): Paaren, Herbert E.

PATENT ASSIGNEE(S): Tetrionics, Inc., USA

SOURCE: U.S., 14 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 5936105 | A | 19990810 | US 1998-96330 | 19980611 |
| PRIORITY APPLN. INFO.: | | | US 1997-53088P | P 19970613 |

IT 235108-14-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 14-epi-19-nor-vitamin D compds. with cell differentiation activity)

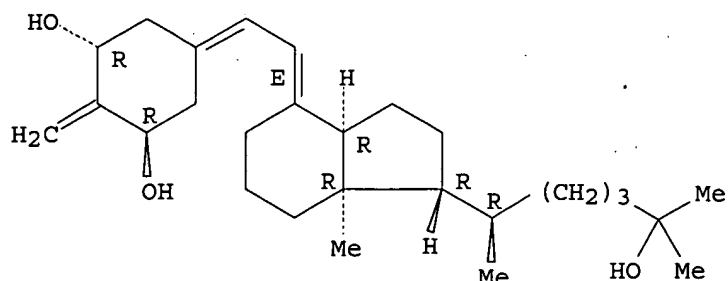
RN 235108-14-2 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-,
(1 α ,3 β ,7E,14 β)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

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AB 14-Epi-19-nor-vitamin D analog compds. are prepared with high cell differentiation and antiproliferative activity and low calcemic activity. More particularly, examples of such compds. include 14-epi-19-nor-1 α ,25-dihydroxyvitamin D₃, 14-epi-20-epi-19-nor-1 α ,25-dihydroxyvitamin D₃ (I), 14-epi-20-epi-19-nor-1 α -hydroxyvitamin D₃, 14-epi-19-nor-1 α ,25-dihydroxyvitamin D₂, 14-epi-19-nor-24-homo-1 α ,25-dihydroxyvitamin D₃, 14-epi-19-nor-20(S)-hydroxymethyl-1 α -hydroxypregnacalciferol, and 14-epi-19-nor-20(R)-hydroxymethyl-1 α -hydroxypregnacalciferol. Thus, I was prepared and showed an EC₅₀ of 0.66 nM to inhibit proliferation of HL-60 cells.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:672847 CAPLUS

DOCUMENT NUMBER: 130:52625

TITLE: New 1 α ,25-Dihydroxy-19-norvitamin D₃ Compounds of High Biological Activity: Synthesis and Biological Evaluation of 2-Hydroxymethyl, 2-Methyl, and 2-Methylene Analogs

AUTHOR(S): Sicinski, Rafal R.; Prahl, Jean M.; Smith, Connie M.; DeLuca, Hector F.

CORPORATE SOURCE: Department of Biochemistry College of Agricultural and Life Sciences, University of Wisconsin-Madison, Madison, WI, 53706, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(23), 4662-4674

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 213319-29-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (synthesis and biol. evaluation of 2-hydroxymethyl, 2-Me, and 2-methylene 1 α ,25-dihydroxy-19-norvitamin D₃ analogs)

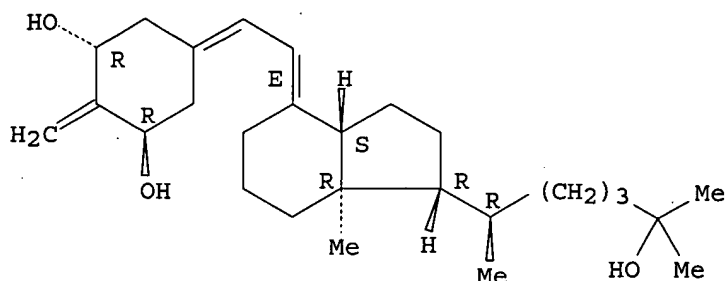
RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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AB New highly active isomers of the natural hormone $1\alpha,25$ -dihydroxyvitamin D₃ possessing an exomethylene group at the 2-position were prepared in a convergent manner, starting with (-)-quinic acid and the corresponding (20R)- and (20S)-25-hydroxy Grundmann ketones. These 2-methylene-19-norvitamins were efficiently converted to the 2-Me and 2-hydroxymethyl derivs., some of which exhibited pronounced *in vivo* biol. activity. Configurations of the A-ring substituents were determined by ¹H NOE difference spectroscopy as well as by spin decoupling expts. It was established that the bulky Me and hydroxymethyl substituents at C-2, due to their large conformational free energies, occupy mainly equatorial positions. Addnl., hydroxylation of the C(10)-C(19) double bond in $1\alpha,25$ -(OH)₂D₃ was performed, resulting in $1\alpha,19,25$ -trihydroxy-10,19-dihydrovitamin D₃ derivs. in which the hydroxymethyl substituent at C-10, for steric reasons, is forced to occupy an axial position. In consequence, the vitamin D₃ analogs were synthesized in which the 1α -hydroxy group, required for biol. activity, is almost exclusively axially or equatorially oriented because of stabilization of the single A-ring chair conformations. The relative ability of the synthesized analogs to bind the porcine intestinal vitamin D receptor was assessed and compared with that of the natural hormone. It was established that vitamins possessing the axial orientation of the 1α -hydroxy substituent exhibit a significantly increased receptor binding affinity. Compds. with a 2-methylene substituent showed selective calcemic activity profiles, being extremely effective on bone calcium mobilization. 2α -Methyl-substituted vitamins proved to be much more active *in vivo* than the corresponding epimers with 2β -configuration. All of the 2-substituted vitamins exhibited pronounced HL-60 differentiating activity, those 2α -substituted in the 20S-series being especially potent. The present studies imply that the axial orientation of the 1α -hydroxy group is necessary for biol. activity of vitamin D compds.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

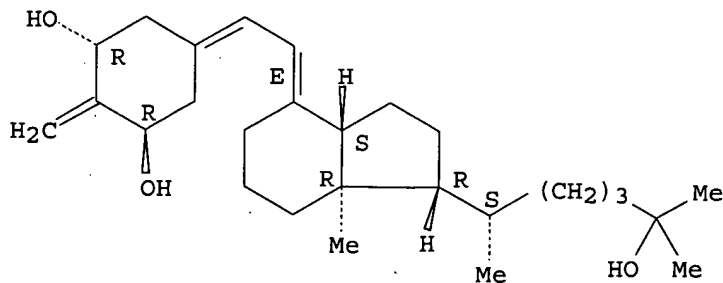
L10 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1998:635741 CAPLUS
 DOCUMENT NUMBER: 129:245333
 TITLE: Preparation of 2-alkylidene-19-nor-vitamin D compounds
 INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.
 PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

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| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|-------------------|-----------------|-------------|
| WO 9841501 | A1 | 19980924 | WO 1998-US2976 | 19980211 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5843928 | A | 19981201 | US 1997-819693 | 19970317 |
| CA 2283829 | A1 | 19980924 | CA 1998-2283829 | 19980211 |
| CA 2283829 | C | 20060711 | | |
| AU 9862801 | A | 19981012 | AU 1998-62801 | 19980211 |
| AU 714253 | B2 | 19991223 | | |
| EP 970047 | A1 | 20000112 | EP 1998-905102 | 19980211 |
| EP 970047 | B1 | 20020911 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| NZ 337503 | A | 20000929 | NZ 1998-337503 | 19980211 |
| JP 2001504135 | T | 20010327 | JP 1998-540501 | 19980211 |
| JP 3786713 | B2 | 20060614 | | |
| AT 223890 | T | 20020915 | AT 1998-905102 | 19980211 |
| ES 2179451 | T3 | 20030116 | ES 1998-905102 | 19980211 |
| PT 970047 | T | 20030131 | PT 1998-905102 | 19980211 |
| NO 9904398 | A | 19990910 | NO 1999-4398 | 19990910 |
| NO 322535 | B1 | 20061023 | | |
| JP 2006117680 | A | 20060511 | JP 2005-319365 | 20051102 |
| PRIORITY APPLN. INFO.: | | | US 1997-819693 | A 19970317 |
| | | | JP 1998-540501 | A3 19980211 |
| | | | WO 1998-US2976 | W 19980211 |
| OTHER SOURCE(S): | | MARPAT 129:245333 | | |
| IT 213250-70-5P | RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of 2-alkylidenenor-vitamin D compds.) | | | |
| RN 213250-70-5 | CAPLUS | | | |
| CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.
Double bond geometry as shown.



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y1, Y2 = H, protecting group; R6, R8 = H, alkyl, hydroxyalkyl, fluoroalkyl, or R6R8 = (CH₂)_x; x = 2-5 integer; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared. Thus, 1 α ,25-dihydroxy-2-methylene-19-norvitamin D₃ (II) was prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at the 3 and 5 positions, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO₄ oxidation, condensation of 3,5-bis(tert-butyldimethylsilyloxy)-4-methylenecyclohexanone with Me₃SiCH₂-COOMe, DIBAL reduction, reaction with Ph₂PH, H₂O₂ oxidation, condensation with perhydroindanone III in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II at 130 pmol/day/7 days were 5.3 \pm 0.4 S/M and 9.9 \pm 0.2 mg/100 mL, resp., vs. 6.2 \pm 0.4 S/M and 7.2 \pm 0.5 mg/100 mL, resp., for 1,25-(OH)₂D₃. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:635740 CAPLUS

DOCUMENT NUMBER: 129:245332

TITLE: Preparation of 2-alkyl-19-nor-vitamin D compounds and their biological activities

INVENTOR(S): Deluca, Hector F.; Sicinski, Rafal R.

PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9841500 | A1 | 19980924 | WO 1998-US2975 | 19980211 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GW, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5945410 | A | 19990831 | US 1997-819694 | 19970317 |
| CA 2272745 | A1 | 19980924 | CA 1998-2272745 | 19980211 |
| CA 2272745 | C | 20051206 | | |
| AU 9862800 | A | 19981012 | AU 1998-62800 | 19980211 |

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|---|----|----------|----------------|----------|
| AU 714390 | B2 | 19991223 | | |
| EP 971888 | A1 | 20000119 | EP 1998-905101 | 19980211 |
| EP 971888 | B1 | 20031029 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| BR 9808010 | A | 20000308 | BR 1998-8010 | 19980211 |
| NZ 337262 | A | 20000929 | NZ 1998-337262 | 19980211 |
| JP 2000513010 | T | 20001003 | JP 1998-540500 | 19980211 |
| JP 3786712 | B2 | 20060614 | | |
| AT 253046 | T | 20031115 | AT 1998-905101 | 19980211 |
| PT 971888 | T | 20040331 | PT 1998-905101 | 19980211 |
| ES 2206893 | T3 | 20040516 | ES 1998-905101 | 19980211 |
| NO 9904489 | A | 19990916 | NO 1999-4489 | 19990916 |
| NO 321925 | B1 | 20060724 | | |
| US 2004072804 | A1 | 20040415 | US 2003-673618 | 20030929 |
| US 6939868 | B2 | 20050906 | | |
| JP 2006096759 | A | 20060413 | JP 2005-319359 | 20051102 |

PRIORITY APPLN. INFO.:

| | | |
|----------------|----|----------|
| US 1997-819694 | A | 19970317 |
| JP 1998-540500 | A3 | 19980211 |
| WO 1998-US2975 | W | 19980211 |
| US 2001-45941 | B3 | 20011019 |

OTHER SOURCE(S): MARPAT 129:245332

IT 213250-70-5P 213319-29-0P

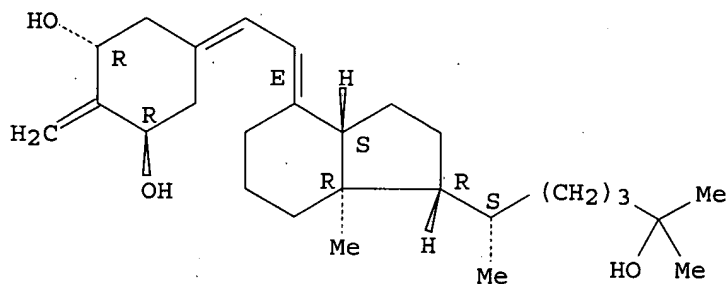
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 2-alkylnor-vitamin D compds. and their biol. activities)

RN 213250-70-5 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E,20S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

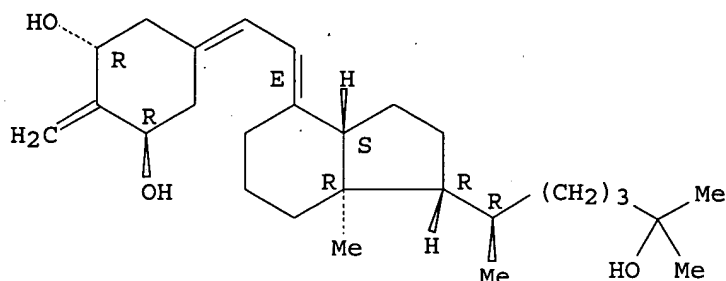


RN 213319-29-0 CAPLUS

CN 19-Nor-9,10-secocholesta-5,7-diene-1,3,25-triol, 2-methylene-, (1 α ,3 β ,7E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

QAZI



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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Y1, Y2 = H, protecting group; R6 = alkyl, hydroxyalkyl, fluoroalkyl, etc.; R = any of the typical side chains known for vitamin D type compds., e.g. Q] are prepared. Thus, 1 α ,25-dihydroxy-2 α - and 1 α ,25-dihydroxy-2 β -methyl-19-norvitamin D3 (II) were prepared in 11 steps from (-)-quinic acid via tert-butyldimethylsilyl protection of the OH groups at positions 3 and 5, converting to protected quinic acid Me ester, oxidation of the 4-OH, methylenation using methyltriphenylphosphonium bromide, hydride reduction, NaIO₄ oxidation, condensation of the resulting 3,5-bis(tert-butyldimethylsilyloxy)-4-methylcyclohexanone with Me₃SiCH₂COOMe, DIBAL reduction, reaction with Ph₂PH, oxidation, condensation with perhydroindanone

III

in the presence of BuLi, and deprotection. These 2-substituted compds. are characterized by low intestinal calcium transport activity and high bone calcium mobilization activity resulting in novel therapeutic agents for the treatment of diseases where bone formation is desired, particularly low bone turnover osteoporosis. The intestinal calcium transport and serum calcium (bone calcium mobilization) activities in rats responding to chronic doses of II (both epimers) at 130 pmol/day/7 days were 5.0 \pm 0.3 S/M and 6.1 \pm 0.1 mg/100 mL, resp., vs. 6.2 \pm 0.4 S/M and 7.2 \pm 0.5 mg/100 mL, resp., for 1,25-(OH)₂D₃. These compds. also exhibit pronounced activity in arresting the proliferation of undifferentiated cells and inducing their differentiation to the monocyte thus evidencing use as anti-cancer agents and for the treatment of diseases such as psoriasis.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S L10 AND AND dELUCA

MISSING TERM 'AND AND'

The search profile that was entered contains a logical operator followed immediately by another operator.

=> S L10 AND DELUCA/AU

0 DELUCA/AU

L11

0 L10 AND DELUCA/AU

=> S L10 AND DELUCA

44 DELUCA

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